The Potential of Saviour Siblings as a Use of Stem Cells

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ABSTRACT

Stem cell research involves using pluripotent cells in a multitude of different ways including repairing tissue damage and testing new drugs, as well as gene therapy methods. In this paper, we aim to explore the concept of Saviour Siblings, their future uses and possible involvement in medical treatment, and the hurdles that will need to be overcome. Given that technology continues to advance in the exponential manner at which it is currently progressing, the obstacle of inefficiency that blocks the path for Saviour Siblings could be bypassed, leaving only the ethical barriers from it becoming a fully fledged treatment option with a wide expanse of uses. Based upon this hypothesis, we believe that Saviour Siblings have the potential to play a large role in the future of medicine.

INTRODUCTION

Arguably, since the development of pharmacology from natural remedies like the bark of the cinchona to modern synthesised pharmaceuticals such as beta-blockers, medicine has become very focussed on effective drug based cures, a different approach from the role of a traditional doctor. Physicians including Thomas Sydenham (1624-1689) encouraged this shift in paradigm, hoping that in the future every disease would have a specific medicinal remedy. In today’s society, however, developing and synthesising new drugs is becoming harder and harder; some people, like author Roy Porter, attribute this to overregulation of the industry [1]. Another issue that plagues the pharmacology industry is the growth of antibiotic resistance in bacteria. This can render antibiotics useless and promote the development of “superbugs”, evidence of which can be found from the emergence of Completely Drug Resistant Tuberculosis in India, where patients cannot be treated because no drugs are effective against the disease [2]. This inappropriate regulation of pharmacology, a result of factors such as disastrous side effects that had not been noted before the drug was approved, has inhibited bold drug innovation. An example of this can be found in the drug diethylstilbestrol (DES), a synthetic oestrogen given to women to prevent miscarriage introduced in the 1940s. It was later found, in 1971, that DES could cause reproductive problems, including vaginal cancers, in ‘DES daughters’ [3]. Just as Sydenham hoped for the pharmaceutical revolution, many scientists today are looking forward to genetically and stem cell focused research and therapies in the near future.

Broadly, there are two different ‘types’ of stem cell: embryonic and adult. Adult (and foetal) stem cells are found in abundance all over the body in specific organs and tissues such as the brain, peripheral blood and liver. The region in which they are found is key to their function; for example, it is easier to stimulate cardiomyocyte stem cells to differentiate into cardiac muscle than it is to use bone marrow stem cells for the same purpose. The term for this is “tissue-specific”, meaning that the cells are found in specific tissues in our bodies and repair the same tissue/organ in which they are found. By contrast, embryonic stem cells are much more flexible in terms of the number of different types of tissue that they can repair. The difficulty arises in trying to stimulate these cells to develop into a particular tissue – adult stem cells differentiate much more readily. Moreover, there have been
cases in the past where embryonic stem cells have transformed into cancerous tissue after transplantation [4]. Nonetheless, should an effective and safe technique be developed in the future, embryonic stem cells will be incredibly useful. A notable exception to this, however, is umbilical cord blood stem cells which are similar to those of adult bone marrow in that they are used to treat diseases of the blood and are thus tissue-specific. The advantage of using this type is that they can be extracted without damaging the embryo since most umbilical cords are taken out and discarded at birth. An interesting grey area between the two main types of stem cell involves “Induced Pluripotent Stem Cells”. These consist of normal body cells that have been modified in such a way that genes which are normally active in embryonic stem cells have been switched on, with the result being that the cell behaves in a similar fashion to embryonic stem cells and is able to differentiate into a variety of different types of tissue. The techniques used for this, however, remain relatively primitive and it will be some time before we can create such cells effectively.

Genetic diseases are very difficult to treat and in most cases impossible to cure with our current knowledge of medicine. Cystic Fibrosis is one of the UK’s most common life threatening inherited disease and affects 9000 people in the UK. In the condition, a thick and sticky layer of mucus builds up inside the lungs, making breathing and digestion difficult. Currently there is no cure and people living with CF have to undergo frequent physiotherapy to clear mucus from the lungs. The only medical treatment available is drugs such as Bronchodilator drugs which open up airways in the lungs by relaxing surrounding muscles to allow easier respiration. Another tragic genetic disease that affects the lives of millions is cancer. Cancer is a term used to describe diseases in which abnormal cells divide uncontrollably to produce tumours which can become malignant and can metastasise to vital organs, causing death. In 2009 156,090 people died from a cancer in the UK [6] and it is thought to be the most common fatal disease in the Western world. At present it can be treated using three methods: a tumour can be surgically removed from the body; the cancerous cells can be targeted with radiation to kill them; or chemotherapy drugs which kill rapidly dividing cells can be used. Despite the fact that these treatments can be fairly effective, they – especially chemotherapy – often cause considerable side effects such as pain and stress to the sufferer. However with both of the examples given stem cells could be used in a bid to treat the symptoms. For example, stem cells could be used to differentiate into cilia which could help remove mucus in the lungs of patients with CF. Moreover, organs from Saviour Siblings could be used to replaced a cancerous organs. Thus it can be seen that whilst gene therapy potentially holds a cure to treating genetic diseases, stem cells can be used to treat symptoms should this not work.

When a foetus is developing, stem cells differentiate into the different parts of the body. At birth the umbilical cord is comprised of stem cells which can be extracted and encouraged to divide and then differentiate into the specific cell needed. For stem cells to be used successfully, they need to be matched to the patient otherwise they will be rejected by the body. Because the cells are genetically very similar to the patient, there would be no fear of the tissue being rejected by the body and so transplantations and transfusions could take place without the ever-present risk of attack from the immune system and the occurrence of Graft vs. Host Disease. The reason the organ would be almost
identical is because each zygote is screened and only the closest match is allowed to develop. Naturally, the zygote chosen will not carry the same problem of the living person. The chosen zygote is then inserted back into the mother or other suitable carrier (possibly even a fermenter, but this would mean the ‘sibling’ would remain a ball of cells rather than develop into a human and so this method of producing Saviour Siblings is not currently being used) for the baby using IVF treatment. Once the baby is born stem cells are used to treat the ill person.

Twelve year old Charlie Whitaker suffered from Diamond Blackfan Anaemia, a condition which prevented him from producing his own red blood cells. He required a blood transfusion every two weeks and realistically a stem cell transplant was his only option to cure him. Since his mother, father and sister were not a genetic match to him, a ‘designer baby’ was the only way for a stem cell transplant to be successful. Jamie Whitaker (Charlie’s Saviour Sibling) is an instance of a successful Saviour Sibling in the UK, or rather in the U.S. The use of a screened embryo to be used in IVF was refused in the UK at that time so the Whitakers flew to America where the procedure was legal. Another instance of Saviour Siblings in the UK was of nine year old Megan Mathews who had Fanconi Anaemia. She too required common blood transfusions and had no known matches. After receiving her little brother Max’s umbilical stem cells, she now requires weekly check ups at Addenbrookes hospital in Cambridge.

In the UK, around 1,000 people die every year because they have been waiting for an organ transplant or because they have become too ill to survive an operation and so the use of Saviour Siblings could massively reduce the waiting times for organ transplants, some of which are currently very long in the UK – the median waiting time for receiving an adult kidney transplant is 1,110 days. Thus it can be seen that these benefits could reduce waiting times for transplant; save money by reducing the number on interventional therapies like dialysis; and save the lives of numerous people.

**DISCUSSION**

Cloning is a rapidly advancing field and has been since the famous ‘Dolly the Sheep’ in 1996. Having analysed the technique being used to clone organisms, we propose that a similar technique could be used to produce Saviour Siblings. The method in question is based on somatic nuclear transfer, or “therapeutic cloning” as it is also known. It involves removing the nucleus from a donor ovum and replacing it with the removed nucleus from a somatic cell of the patient requiring a stem cell

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Figure II [9]

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transplant. This creates a diploid zygote that is genetically identical to stem cells of the patient. This can then be stimulated to form a blastocyst, which has an inner layer called the inner cell mass, with a high concentration of stem cells. These can be isolated from the blastocyst; embryonic stem cell lines can be formed and then infused into the patient to carry out whatever process is necessary [10].

One benefit of this type of cloning is that no surrogate mother is required as would normally be the case, because the embryo would not be intended to grow into a foetus, and so this would make the process slightly easier, as finding a willing surrogate mother could prove difficult. One major advantage to this method of obtaining stem cells is that they are pluripotent and so can be applied in a large variety of cases, being able to divide into any type of body cell. Because the cells are genetically identical to the patient, there would be no fear of the tissue being rejected by the body and so transplantations and transfusions could take place without the ever-present risk of attack from the immune system. One major flaw to therapeutic cloning is that it takes many attempts to produce a viable egg that is stable enough to form a blastocyst and it can require hundreds of attempts before a successful fusion. This poses a large problem because finding donor ova can prove problematic and a steady demand would need to be fulfilled for this procedure to make a significant impact. A more efficient method of infusing the somatic nucleus with the donor ovum would be necessary for therapeutic cloning to get off the ground. Another large issue is the ethical stigma attached to embryonic stem cell research, and these ethical issues will be discussed as a whole later on in the discussion.

Currently, the law in the United Kingdom states that doctors can take stem cells from the umbilical cord or bone marrow of babies who are a genetic match of their siblings for use in transplants. There have been several movements to review the laws regarding the use of Saviour Siblings, which most recently culminated in a bid by MP David Burrowes to completely ban tissue typing in 2008; this, however, was defeated by a vote of 163 in favour to 342 opposing. The current Secretary of State for Health Andrew Lansley also sought reform in 2008 to only allow tissue typing and sex selection in cases where the other sibling is suffering a life threatening illness – again, this was defeated by 318 votes to 149 [11]. This demonstrates faith in stem cell research as a possible therapy in the future. Moreover, depending on the success or failure of experiments in the near future, the law regarding the use of Saviour Siblings could change. There are currently restrictions on the number of oocytes that a female donor can donate for medical research, which is unhelpful for scientists who require these female gametocytes for furthering the fields of stem cell research [12]. However, laws on donation could be further tightened in the near future, as egg donors are set to have their compensation tripled. This raises several ethical issues, as it puts forward the impression that women should donate for purely selfish reasons, as opposed to the altruistic approach that some feel should be taken when donating something. Some argue that this also devalues the worth of what is essentially half of a potential human being, claiming that donation could become a financial incentive [13]. Dr. David King, Director of Human Genetics Alert, argues, “Ethically, it’s wrong to make part of the human body a commodity”, reinforcing the viewpoint women should donate because they wish to further scientific research, rather than for a monetary incentive. The backlash over the proposal to increase compensation could cause for the laws on oocyte donation to be re-drawn and adds an element of uncertainty to how quickly and easily stem cell research will be able to develop.

One controversial use of Saviour Siblings is in drug trials. Currently it takes 10 to 15 years to trial and introduce a new drug into the market. During this long period, patients die whilst waiting for a drug that may cure them. Moreover, despite such a vigorous approach, there are still instances in which the drug produced causes severe adverse effects to the patient. For example, according to the Drug
Controller General of India’s records, 25 people died in clinical trials in 2010. Even in England, six men were entered into intensive care after a drug trial went wrong in 2006 [14]. A possible solution to this problem is using Saviour Siblings. Animals, despite having a similar genetic make-up to humans, are different to us and so what may not affect them may still affect us. By contrast, Saviour Siblings are, in terms of genetics at least, human. Therefore one may assume that they will react in the same way as adult humans to a particular drug. Using them instead of animals will reduce/stop animal testing and will ensure that the drug is tested more vigorously before it enters the Human testing stage; this means it will be safer for volunteers. Furthermore, since stem cells have no Hayflick limit, we could always extract tissue from Saviour Siblings and grow them on a commercial scale and then use this tissue to test drugs. This would decrease the cost it takes to obtain tissue samples for drug testing – currently drug trials may cost over one billion dollars [15].

The real advantage of using Saviour Siblings is that, because cells being given by the ‘sibling’ are very similar to those of the patient, there is less risk of rejection or the occurrence of Graft vs. Host disease. Plus, as has already been explained, the ‘sibling’ may be able to continue and develop into a person. There is a danger, however, of this idea soon spiralling out of control. There have been several instances on sci-fi shows of wealthy individuals making clones of themselves to provide compatible body parts for when they get ill, most notably in The Island (2005) and recently in the TV series Smallville. This horror-movie scenario does, however, have some scientific backing. Foetuses develop eight weeks after initial fertilisation and, although (arguably) not alive, they have differentiated cells which soon develop into organs. It may be possible to allow the foetus to develop until it is mature and then to take fully developed organs out and use them for transplant. The foetus could then be stored cryogenically (so as to not let it develop any further and become a ‘proper’ human) and could remain as an organ bank. Naturally, such an experiment has not been carried out yet, but there seems no reason to believe that it would not work. Despite progress, 8,000 people were in need of an organ transplant in the UK in 2010. If other uses of stem cells and Saviour Siblings take too long to develop, the highly pertinent question arises – in light of the high demand for organs – as to whether the benefits of using Saviour Siblings in such a manner would outweigh the risks.

Our argument so far has demonstrated the potential use of Saviour Siblings in the future. Indeed, most of the technology necessary to advance is already available, or should become available in the coming years. Thus what is limiting the use of Saviour Siblings is not science but rather ethics. The “slippery-slope” argument is ever-present in books about medical ethics. Its premise is that one should always be wary because there is always a risk of something that seems good turning bad. Specifically, with regards to Saviour Siblings, whilst they are of undeniable use and an advantage to those whose lives will be saved, it is necessary to be cautious. Saviour Siblings have enormous benefits but there is a very real threat of people misusing them. Nightmare scenarios of people keeping living organ banks in a cryogenic state could become a reality and due to the advances in healthcare that Saviour Siblings could bring, people may be able to carry on living well past their 80 or so years. If people develop liver cancer, they can just replace their liver instantly, before the cancer starts to develop. In such a way, people will live longer – an ageing population could have repercussions on a social and an economic scale.

There is an argument from a religious/moral perspective that the Saviour Sibling is a human in its own right and deserves to develop rather than be kept half-alive. A human being should never be “a commodity rather than a person” [16] and this argument also contradicts Kant’s famous dictum, “never use people as a means but always treat them as an end.” Indeed, the pertinent question arises, therefore, as to whether the incredible scientific advances Saviour Siblings can bring is worth
devaluing the sanctity of human life. However, couples frequently try and conceive a child in order to provide company for an existing child; how is treating a child as a means in this regard that much different to using the child as a Saviour Sibling? Indeed, one can argue that any conceivable risk is outweighed by the immense benefits that Saviour Siblings can provide.

**CONCLUSION**

Saviour Siblings have the potential to bring with them a landslide of new treatments, as well as a source of tissue that could be used to test new drugs and therapies. Whilst the evident ethical hurdles that would need to be traversed are hard to overcome, and the possibility that the introduction of Saviour Siblings as a viable treatment option could bring about a “slippery slope”, this innovative concept has many possible uses and has already been used successfully. Moreover, the “slippery slope” argument is generally fundamentally flawed because it claims that since the last link in a chain is undesirable – in this case that a Saviour Sibling might be created simply as an organ bank and kept in a cryogenic state until needed – the first link in the chain is equally undesirable. However, this is not always the case; in this example, the first link – using Saviour Siblings – in the chain can occur without it necessarily leading to the dystopian future that some people predict. This commits the argument to the “slippery slope fallacy”, thus weakening the argument. There will always be ethical barriers ahead of genetic advancement unless basic human ideology towards creating life is adapted and changed over time.

Problems with the efficiency of the embryo selection process when choosing the right genetic match to the patient will plague the advancement of Saviour Siblings until technology progresses in such a way that this can be overcome. Whilst there is always the risk that the embryo chosen will not match the patient, opening the road to rejection from the host, this risk is highly likely to improve with developments in genetic screening and in-vitro fertilisation.

The public have been notoriously influenced by inflammatory reports in the news in the past, most notably against genetically modified foods. This means that, should we decide that Saviour Siblings are the way forward, we will need to work extremely hard to convince the public. To prevent the slippery-slope scenario as well as other ethical problems, there needs to be new international legislation that sets a legal precedent by which countries and bodies can advance with necessary caution. Such laws need to be clear and should factor in ethical concerns without substantially limiting scientific progress. An international body such as a more powerful version of the HFEA should be created and should oversee such affairs by liaising with the scientific community. Only in such a way can the use of Saviour Siblings become widespread (but controlled) and really benefit mankind in an unprecedented fashion.

**APPENDIX**

[3] – Article referencing the side effects of Diethylstilbestrol
http://www.cdc.gov/DES/consumers/about/effects_daughters.html

[4] – Definition of different types of stem cells
http://www.closerlookatstemcells.org/Stem_Cell_Types.htm

[5] – Figure I – Representation of differentiation of stem cells

[6] – Statistics relating to the mortality rates of different cancers
http://info.cancerresearchuk.org/cancerstats/mortality/all-cancers-combined/newpagetemp

[7] – Article on Saviour Sibling success
http://www.telegraph.co.uk/health/healthnews/8499394/Saviour-sibling-cures-sick-older-brother.html

[8] – Statistics relating to transplants
http://www.uktransplant.org.uk/ukt/newsroom/fact_sheets/transplants_save_lives.jsp

[9] – Figure II – Representation of Somatic Nuclear Cell Transfer


[11] – Article referencing movements in parliament to ban Saviour Siblings
http://news.bbc.co.uk/1/hi/uk_politics/7409264.stm

[12] – Research paper referencing oocyte donation
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2323472/


http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2630351/

[16] – Article relating to the ethics of two cases of Saviour Sibling use
http://www.prochoiceforum.org.uk/irl_rep_tech_2.php